

## **REMARKS**

### **1. Objections to the Claims**

The Examiner objects to claims 1-5, 7, 8, and 23, because the claims contain non-elected inventions such as antibody and non-elected antigens NCAM, CEA, Lewis b, sialyl-Tn, and Globe H.

Applicants respectfully submit that, as discussed in the response of September 10, 2007, the restriction requirement is an improper attempt to limit Applicants to a species and is an improper application of the procedure for examination of generic and Markush-type claims. Applicants continue to assert that they are entitled to examination of additional species and of the generic claims, once claims to the elected species are found allowable over the prior art.

### **2. Claim rejections, 35 U.S.C. § 103**

The Examiner rejects claims 1-5, 7, 8 and 23 under 35 U.S.C. §103 as being unpatentable over WO 01/35989 A2 in view of Maruyama et al., Sabatinni et al., and Berthelsen et al.. The Examiner states that Maruyama teaches a cancer vaccine comprising the antigen GA733 (EPCAM) while Sabatinni teaches at vaccine comprising Lewis Y antigen for treating ovarian cancer. The Examiner states that WO/135989 A2 teaches a vaccine comprising an anti-idiotypic antibody for EpCAM, and anti-idiotypic antibody for Lewis Y or anti-idiotypic antibodies for both. Therefore, the Examiner concludes, one skilled in the art would expect that EpCAM and Lewis Y antigens can be used together for treating cancer, given the fact that they induce immune response to the same proteins. Applicants respectfully disagree.

#### **2.1 The Prior Art Teaches Away From the Present Invention**

Applicants put forth significant reasons why one in the field would not have considered treatment with a combination of antigen tumor therapy therapeutic agents (especially when non-specific reactions, such as cross-reactivity, could be expected), in the reply dated September 10, 2007. Therefore, Applicants will not repeat their arguments here. However, Applicants submit

that the Examiner's disregard for the differing immunological response to treatment with anti-idiotypic antibodies as opposed to the actual tumor associated antigen improperly dismisses the evidence presented in Luo and Kieber-Emmons. One skilled in the art would not disregard possible side effects or ineffectiveness in a combination therapy, thus the present claims are not obvious in light of the prior art. Applicants request the Examiner withdraw the rejection.

### 2.2 The Invention Demonstrates New and Unexpected Results Relative to the Prior Art

Applicants also submit that the invention as claimed is not obvious because the combination therapy of the present invention has an unexpected and surprising synergistic effect, resulting in a particularly efficient treatment. The Examiner states that applicants have failed to provide evidence that the combination of EpCAM and Lewis Y antigens provide synergistic effect. Applicants respectfully point the Examiner's attention to Figure 4 in the specification, which shows a synergistic effect for the combinations of anti-Lewis Y antibody IGN311, and the anti-EpCAM antibody Herceptin. These results demonstrate that this combination is substantially superior over the effects of IGN311 alone (first graph) and Herceptin alone (second graph). (See also, Specification pages 30-32).

In particular, the hill-slope of the combined therapies increased, indicating a synergistic effect. (Specification, page 31, line 8-14). One skilled in the art would recognize that an increased hill-slope suggests a synergistic relationship, as indicated by the excerpt of "Fluorescence Polarizing Technical Resource Guide," Chapter 7, "Theory of Binding Data Analysis". (provided herein). Page 6, last paragraph, of this Guide explains that the relationship of slope and cooperativity, i.e., synergistic effect.

The Examiner states that "the use of a vaccine comprising two or more tumor-associated antigens is well known in the art, as shown by the teaching of Spitler." The Examiner indicates that it is prima facie obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very

same purpose.” Applicants submit that even if the prior art references support a prima facie case of obviousness, Applicant’s unexpected results successfully rebut that case. Applicants point out that the Specification, as filed, expressly indicates that the “[c]ombination of IGN311 and Herceptin® leads to an enhanced lysis potential, gr[e]ater [sic] than the effect that would have been observed by the sum of the individual components.”

Furthermore, the Examiner’s statement that “the combination of drugs that possesses the therapeutic effects of each individual drug would still provide motivation to one skilled in the art because the combination is at least more effective than the single drug.” Applicants respectfully submit that this conclusion is simply speculation. As shown by the evidence presented in Luo and Kieber-Emmons, one skilled in the art would not expect carbohydrate Lewis Y to induce a T-cell dependent response. Combining an EpCAM antigen with a carbohydrate Lewis Y antigen *at best* could be expected to be as effective EpCAM antigen alone and/or Lewis Y antigen alone, but *at worst* could lead to a non-specific immune response or harmful side effects. Thus, the unexpected synergy of the present treatment is non-obvious.

Applicants respectfully request the Examiner withdraw the rejection and allow all claims.

### **CONCLUSION**

In view of the above amendment, Applicants believe the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson, Reg. No. 30,330 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Application No. 10/524,516  
Amendment dated May 6, 2008  
After Final Office Action of November 6, 2007

Docket No.: 4518-0109PUS1

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

Dated: May 6, 2008

Respectfully submitted,

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